UNIT 7 - APPLICATION OF THEORY IN PRACTICE PART 1

Precision Healthcare: Genomics-Informed Nursing by Andrea Gretchev

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Unit 7 Contents

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7.1 UNIT OVERVIEW

Learning Objectives

- Apply course content to practice scenarios

Practice questions and case studies are provided for independent practice for students to apply what they have learned thus far in the course. Please see Blackboard for the group discussion assignment for this week which will also provide an opportunity to apply learning.

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7.2 APPLICATION OF THEORY - READINGS & CASE STUDIES

Optional Reading

This article uses a case study of a family with a history of breast and prostate cancer to highlight the importance of coordinated genetic care by genetics professionals. The article argues that fragmented genetic care can lead to errors such as inappropriate testing, miscommunication of results, and missed opportunities for cancer prevention and early detection, ultimately resulting in psychosocial distress and increased healthcare costs.

Read

Mahon S. M. (2019). Coordination of genetic care: More important and complicated than it seems. *Journal of the National Comprehensive Cancer Network*, *17*(11), 1272–1276. https://doi.org/10.6004/jnccn.2019.7343

OPEN ACCESS ONLINE

Case Study – Clinical Application

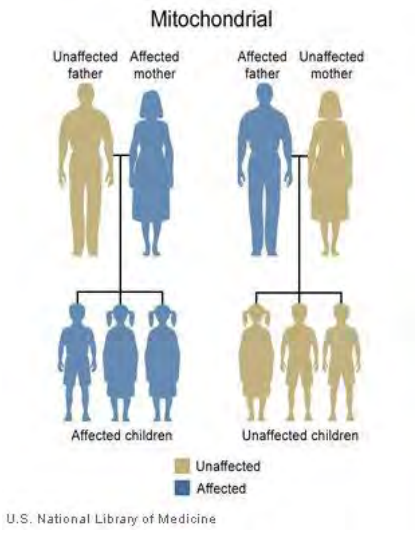
Mitochondrial DNA mutation A1555G and aminoglycoside-induced hearing loss and deafness Case study – a mitochondrial DNA variant causes susceptibility to hearing loss on administration of aminoglycosides.

Key Takeaway:
Carriers of the mutation who undergo even one course of aminoglycoside antibiotic therapy can suffer severe an irreversible loss of hearing.

Clinical Scenario:

A term newborn is noted to have an elevated temperature (39 C) and an elevated respiratory rate (45/minute). Sepsis is suspected, blood cultures and laboratory studies are obtained and the child is moved to the intermediate care unit for IV antibiotics (Clinical guidelines recommend Ampicillin and Gentamicin for rule out sepsis). When the mother is informed of the need to start antibiotics she tells the care team that she has hearing loss that she says occurred after receiving an antibiotic that she doesn't remember. "Some kind of mycin I was told," She is very concerned that this could happen to her child and asks that the baby be 'checked out'.

A quick PubMed search using the terms 'antibiotics' and 'hearing loss' identifies many articles that discuss the risk of hearing loss in individuals exposed to aminoglycoside antibiotics that have a specific mitochondrial pathogenic variant. Given this information the decision is made to start the baby empirically on Ampicillin and a cephalosporin and pursue investigation of the mitochondrial variant.



Source: National Human Genome Research Institute, PDM with attribution.

Description of relevant genomic information and how this information would be used:

Mitochondria undergo a special type of inheritance called maternal inheritance. Only the mother contributes mitochondria to her children. Thus, when a mitochondrial DNA mutation occurs in one of the maternal mitochondrial genes, she will pass it to all of her offspring. Males do not pass mitochondria to any of their offspring. Mitochondria are involved in the intermediate metabolism of many ingested substances and drugs. Mutations in two mitochondrial genes, MT-RNR1 and MT-TS1, confer susceptibility to non-syndromic mitochondrial hearing loss or deafness after treatment with aminoglycoside antibiotics (e.g. gentamicin, kanamycin, streptomycin). Specifically a change from alanine to glycine in position 1555 ("A1555G mutation") in the MT-RNR1 gene has been associated with aminoglycoside-induced (as well as late onset non-syndromic) sensorineural hearing loss. There are population differences in the prevalence of the A1555G mutation: 2.9% – 5.3% in Asian, 0.6% – 2.5 % of Caucasian and as high as 17% of the Spanish population with nonsyndromic hearing loss. Therefore, Asian and Spanish populations have the highest frequency of the A1555G mutation followed by other populations of European ancestry. A higher frequency of the mutation is found among the deaf population with a history of aminoglycoside exposure accounting for 15-30%. Both males and females are affected equally. The hearing loss is generally bilateral and in the moderate to profound range. Once exposed to aminoglycoside antibiotics,

most individuals with the variant go on to develop hearing loss or deafness (Usami & Nishio, 2018; Rehm et al., n.d.; Vivero et al., 2012; Xing et al., 2007).

Recommended clinical action: Genetic testing for the A1555G mutation should be performed in individuals with moderate to profound hearing loss in the presence of either a family history of hearing loss suggestive of maternal inheritance or onset of hearing loss following administration of an aminoglycoside antibiotic such as gentamicin. For women who carry the A1555G mutation, with or without hearing loss, carrier testing is recommended for other maternal family members with instructions for their children and all other maternal members to strictly avoid the administration of aminoglycoside antibiotics if they carry the mutation. Carriers of the mutation who undergo even one course of aminoglycoside antibiotic therapy can suffer severe and irreversible loss of hearing. As a cautionary note, lack of identification of the mutation does not rule out hearing loss attributable to other variants within mitochondrial genes (e.g. the MT-RNR1 gene) or due to other genes known to be involved in hearing loss (Guan et al., 2006).

Family Implications: Hearing loss caused by this pathogenic variant (A1555G) is consistent with a maternal pattern of inheritance.

Evidence to support the use of genomic information in this scenario: ACMG Practice Guideline: Genetics Evaluation Guidelines for the Etiologic Diagnosis of Congenital Hearing Loss

Source: Case study: Mitochondrial DNA mutation A1555G and aminoglycoside-induced hearing loss and deafness [PDF] from *Family Health History for Healthcare Professionals* Courtesy: National Human Genome Research Institute (NHGRI), Public Domain with attribution .

Resources:

ACMG (2002). Genetics Evaluation Guidelines for the Etiologic Diagnosis of Congenital Hearing Loss. Genetic Evaluation of Congenital Hearing Loss Expert Panel. ACMG statement. *Genetics in medicine : official journal of the American College of Medical Genetics*, *4*(3), 162–171. https://doi.org/10.1097/00125817-200205000-00011

US Preventive Services Task Force (2008). Universal screening for hearing loss in newborns: US Preventive Services Task Force recommendation statement. *Pediatrics*, *122*(1), 143–148. https://doi.org/10.1542/peds.2007-2210

NIH. (2023, September 28). Genetic hearing loss overview. *GeneReviews*. https://www.ncbi.nlm.nih.gov/books/NBK1434/

PharmGKB. (n.d.). *MT-RNR1 m.1555A>G*. https://www.pharmgkb.org/haplotype/PA166229255

Medline Plus. (2014, May 1). *MT-TS1 gene*. https://medlineplus.gov/genetics/gene/mt-ts1/

Attribution & References

- Case study: Mitochondrial DNA mutation A1555G and aminoglycoside-induced hearing loss and deafness [PDF] from *Family Health History for Healthcare Professionals* courtesy: National Human Genome Research Institute (NHGRI), Public Domain with attribution . / References changed to APA format.

References

Guan, M., Yan, Q., Li, X., Bykhovskaya, Y., Gallo-Teran, J., Hajek, P., Umeda, N., Zhao, H., Garrido, G., Mengesha, E., Suzuki, T., Del Castillo, I., Peters, J. L., Li, R., Qian, Y., Wang, X., Ballana, E., Shohat, M., Lu, J., . . . Fischel-Ghodsian, N. (2006). Mutation in TRMU Related to Transfer RNA Modification Modulates the Phenotypic Expression of the Deafness-Associated Mitochondrial 12S Ribosomal RNA Mutations. *The American Journal of Human Genetics*, *79*(2), 291–302. https://doi.org/10.1086/506389

Rehm, H. L., Williamson, R. E., Kenna, M. A., Corey, D. P., Korf, B. R., & Harvard Medical School Center For Hereditary Deafness. (n.d.). Understanding the genetics of deafness. In *Harvard Medical School Center for Hereditary Deafness*. https://projects.iq.harvard.edu/files/centerforhereditarydeafness/files/understanding_the_genetics_of_deafness.pdf

Usami S, & Nishio S. (2018, June 14). Nonsyndromic hearing loss and deafness, Mitochondrial. In Adam MP, Feldman J, Mirzaa GM, et al., (Eds). *GeneReviews*®. University of Washington. https://www.ncbi.nlm.nih.gov/books/NBK1422/

Vivero, R. J., Ouyang, X., Yan, D., Du, L., Liu, W., Angeli, S. I., & Liu, X. Z. (2012). Mitochondrial DNA mutation screening in an ethnically diverse nonsyndromic deafness cohort. *Genetic testing and molecular biomarkers*, *16*(9), 1146–1148. https://doi.org/10.1089/gtmb.2011.0365

Xing, G., Chen, Z., & Cao, X. (2007). Mitochondrial rRNA and tRNA and hearing function. *Cell Research*, *17*(3), 227–239. https://doi.org/10.1038/sj.cr.7310124

7.3 - APPLICATION: PRACTICING PEDIGREE ANALYSIS

Practicing Pedigree Analysis (text version)

1. **Gender Inclusive Pedigree Symbols**

   Symbols:

   1. a square with an up arrow on the upper left corner
   2. circle with up arrow on the upper left side
   3. triangle with an up arrow on the upper left corner
   4. circle with a cross on the upper left corner
   5. square with a cross on the upper left corner
   6. triangle with a cross on the upper left corner
   7. circle with the letter i on the upper corner
   8. square with the letter i on the upper corner
   9. triangle with the letter i on the upper left corner

Identify the symbols by placing their number in the correct row/column on the chart.

Assigned Gender	Identifies as girl/ woman	Identifies as boy/man	Identifies as non-binary
Assigned female at birth			
Assigned male at birth			
Assigned intersex at birth			

Check your answer in footnote[1]

1. **Gender Inclusive Pedigree Symbols – Activity Solution**

Assigned Gender	Identifies as girl/woman	Identifies as boy/man	Identifies as non-binary
Assigned female at birth	4	5	6
Assigned male at birth	2	1	3
Assigned intersex at birth	7	8	9

Determining modes of inheritance

2. **True or false?** In the pedigree shown (Fig. 7.4a), generation II shows a male with the trait with an affected son. An X-linked trait cannot be passed from father to son. Therefore x-linked dominance can be ruled out as a mode of inheritance. This pedigree shows an autosomal dominant mode of inheritance.

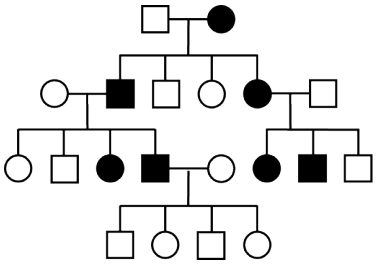


Fig. 7.4a

Check your answer in footnote[2]

3. The pedigree shown (Fig. 7.4b) tracks an X-linked recessive trait. As is typical of X-linked recessive traits, only males appear to be affected. Y-linked traits also only affect males. What feature(s) of this pedigree allow you to rule out Y-linked as a mode of inheritance in this pedigree?

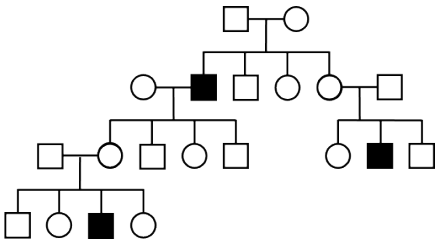


Fig. 7.4b

   a. Y-linked traits pass from father to son, and fathers and sons always share the same phenotype. In the X-linked pedigree shown in this figure, fathers who are affected by the trait have sons who are unaffected. This rules out Y-linkage.
   b. Y-linked traits pass from father to son, and fathers and sons always share the same phenotype. In the X-linked pedigree shown in this figure, fathers who are affected by the trait have sons who are unaffected. This rules out X-linkage.
   c. Y-linked traits pass from father to son, and fathers and sons always share the same phenotype. In the X-linked pedigree shown in this figure, fathers who are affected by the trait have daughters who are unaffected. This rules out Y-linkage.

Check your answer in footnote[3]

4. Match the correct words to the blanks for the pedigree chart in Fig 7.4c:

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2. **True.** An X-linked trait is associated with genes located on the X chromosome. Males have one X chromosome and one Y chromosome (XY), while females have two X chromosomes (XX). When a father contributes genetic material to his child, he passes his Y chromosome to his son, which determines the male sex, and his X chromosome to his daughter. Since sons inherit the Y chromosome from their father, they do not inherit any genes located on the father's X chromosome. Therefore, any X-linked traits or conditions carried by the father cannot be transmitted to his sons. Instead, if the father carries an X-linked trait, it can only be passed to his daughters, as they inherit his X chromosome.

3. a.

Words: affected, unaffected

For a daughter to be [Blank a] by an X-linked recessive trait, she must inherit the X-linked allele from both her father and mother. Her hemizygous father must also be [Blank b] by the trait if he carries the allele. In this pedigree, we see an [Blank c] daughter of an [Blank d] father, which rules out an X-linked recessive mode of inheritance.

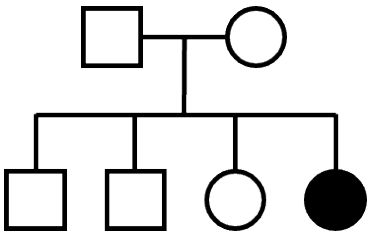

Fig. 7.4c

Check your answer in footnote[4]

5. Why are the offspring of consanguineous matings at higher risk for rare genetic disorders?
   a. Rare recessive disorders are uncommon because the causative alleles are uncommon among the larger population. However, everyone likely carries at least a few rare, disease-associated alleles.
   b. When choosing a partner randomly, it is unlikely (but not impossible) that the partner will share the same set of rare, disease associated alleles.
   c. Close relations may share the same disease-associated alleles, making it more likely for offspring of a consanguineous relationship to inherit two disease-associated alleles of the same gene

   Check your answer in footnote[5]

6. Match the words to the correct blanks, according to the pedigree chart in Fig. 7.4d.

   Words: II-1, aa, Aa

   Individuals I-1 and I-2 must both have genotype [Blank a]*Aa*, since they have an affected child (II-1) who is presumed to have genotype [Blank b]*aa*. This is also true for individual I-3, who has a child with the trait as well. I-4 has the genotype [Blank c]*aa*, since they have the trait.

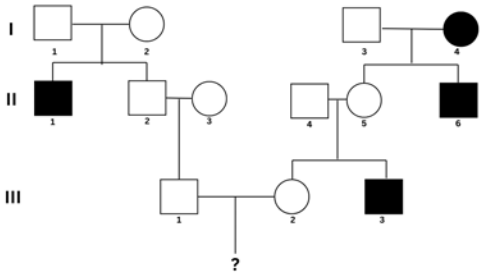

Fig. 7.4d

   Check your answer in footnote[6]

7. Since this is a rare trait in the population, in generation II, we assume that individual II-3 is not a carrier. If this is the case, what is the genotype of II-3? (See Fig. 7.4d)
   a. AA
   b. Aa
   c. aa

   Check your answer in footnote[7]

---

4. Blank a – affected, Blank b – affected, Blank c – affected, Blank d- unaffected

5. a, b & c.

6. Blank a: Aa, Blank b: aa, Blank c: aa

8. True or false? Individuals II-4 and II-5 in Fig. 7.4.d must have genotype AA since they are unaffected (click image to enlarge).
   Check your answer in footnote[8]
9. If the final offspring (see Fig. 7.4d) is affected and exhibits the trait, individual II-2 must be a carrier of the recessive allele "a" since individual II-3 was determined to be AA. What is the probability that they inherited the "a" allele?
   a. 1/4
   b. 3/4
   c. 2/3
   d. 1/3

   Check your answer in footnote[9]
10. Match the words to the correct blanks according to the pedigree chart in Fig. 7.4d.
    Words: 3/4, aa, 1/4
    Assume individuals III-1 and III-2 have parents with the same genotypes. In each of these parental pairs, one parent is homozygous AA and the other is heterozygous (**[Blank a]**). The probability that III-1 and III-2 will be unaffected carriers (genotype As) is **[Blank b]***.
    Check your answer in footnote[10]
11. What is the probability that the offspring of III-1 and III-2 is affected (see Fig. 7.4d). Hint: Both parents are heterozygous.
    2. 3/4
    3. 1/2
    4. 1/4

    Check your answer in footnote[11]

Activity source: Pedigree analysis In *Chromosomes, Genes, and Traits: An Introduction to Genetics* by Amanda Simons, CC BY-NC-SA 4.0

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7. A. AA

8. False. AA is not the genotype for these two individuals. They are Aa since they have an affected child. II-5 inherits a dominant allele from her father and a recessive allele from her mother.

9. c. The probability of Aa is 2/3.

10. Blank a: Aa, Blank b: 1/2.

11. a. There is a 3/4 chance the offspring will be unaffected and a 1/4 chance of being affected.

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7.4 APPLICATION: PRACTICING INHERITANCE PROBABILITIES

Practicing Inheritance Probabilities: Earlobes, Duchenne Muscular Dystrophy, Dimples

An interactive H5P element has been excluded from this version of the text. You can view it online here: https://ecampusontario.pressbooks.pub/personalizedhealthnursing/?p=4457#h5p-52

Practicing Inheritance Probabilities: Earlobes, Duchenne Muscular Dystrophy, Dimples (text version)

1. The pedigree in **Fig. 7.5a** tracks the presence of attached earlobes through a family's generations. Having attached earlobes is an autosomal recessive trait. If individual III-6 married a man who was homozygous for unattached earlobes, what is most likely to be true regarding their children? **Check your answer in footnote**[1]
    a. The children would all have partially attached earlobes.
    b. All the female children will have unattached earlobes, and all the male children will have attached earlobes.
    c. All of their children would have unattached earlobes.
    d. All of their children would have attached earlobes.

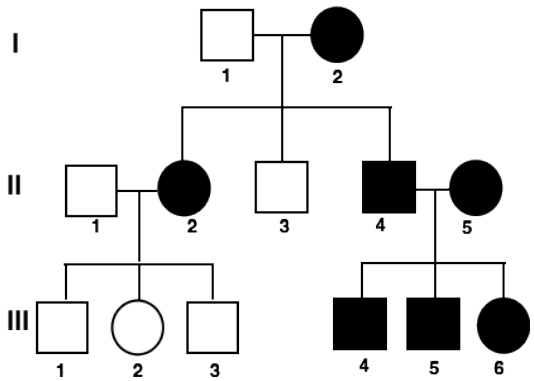

Fig. 7.5a Attached earlobes

2. The pedigree in **Fig. 7.5a** tracks the presence of attached earlobes through a family's generations. Having attached earlobes is an autosomal recessive trait. If individuals I-1 and I-2 had a fourth child, what is the chance that the child would have attached earlobes? **Check your answer in footnote**[2]
    a. 50%

1. c. All of their children would have unattached earlobes.

b. 75%
c. 0%
d. 100%

3. The pedigree in **Fig. 7.5a** above tracks the presence of attached earlobes through a family's generations. Having attached earlobes is an autosomal recessive trait. What is the genotype of individual I-1? **Check your answer in footnote**[3]
   a. ee
   b. X^eY
   c. EE
   d. Ee
4. The pedigree **Fig. 7.5a** above tracks the presence of attached earlobes through a family's generations. Having attached earlobes is an autosomal recessive trait. What is the genotype of individual II-3? **Check your answer in footnote**[4]
   a. ee
   b. X^eY
   c. EE
   d. Ee
5. The pedigree in Fig. 7.5b tracks Duchenne Muscular Dystrophy (DMD) through several generations. DMD is an X-linked recessive trait.

   If individuals I-1 and I-2 had another son, what is the chance that he would have DMD? **Check your answer in footnote**[5]
   a. 0%
   b. 25%
   c. 50%
   d. 100%

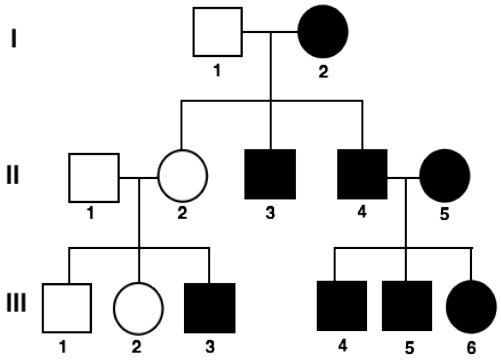

Fig. 7.5b Duchenne Muscular Dystrophy

6. The pedigree in **Fig. 7.5b** tracks Duchenne Muscular Dystrophy (DMD) through several generations.
   DMD is an X-linked recessive trait.Based on the pedigree, which of the following is true? **Check your**

---

2. a. A cross between I-1 and I-2 would produce two offspring with unattached earlobes (**Ee**) and two offspring boxes with attached earlobes (**ee**).

3. d. I-1 must have a heterozygous genotype because he is able to pass on a recessive allele to some of his offspring (II-2 and II-4).

4. d. II-3 must have a heterozygous genotype because he has a mother with attached earlobes, but shows the dominant condition.

5. d. Because individual I-2 is affected, she can only pass on a recessive DMD allele to her sons. This means that all of her sons will have DMD.

answer in footnote[6]

a. Individual II-3 has a genotype of X^DY.
b. If individuals II-4 and II-5 have a fourth child, there is a 50% chance that it will not have DMD.
c. Individual II-1 is a carrier for DMD.
d. If individual III-1 marries an unaffected, non-carrier female, none of their offspring will have DMD.

7. The pedigree in **Fig. 7.5b** tracks Duchenne Muscular Dystrophy (DMD) through several generations. DMD is an X-linked recessive trait.What is the genotype of individual II-2? **Check your answer in footnote**[7]
   a. X^dY
   b. X^dX^d
   c. X^DD^d
   d. X^DX^D
8. The pedigree in **Fig. 7.5b** tracks Duchenne Muscular Dystrophy (DMD) through several generations. DMD is an X-linked recessive trait.If individual II-3 has a child with a carrier woman, what is the percent chance that the child will be a *daughter* with DMD? **Check your answer in footnote**[8]
   a. 100%
   b. 50%
   c. 25%
   d. 0%

6. d. Individual III-1 is an unaffected male. If he mates with an unaffected, non-carrier female, there is no chance that the children will inherit the DMD allele.

7. d. Since DMD is X-linked, individual II-2 needs to be able to pass on a DMD allele to her son. A homozygous dominant genotype would not allow for that.

8. c. In order for a daughter to be affected, she must have a genotype X^dX^d. There is a 1 in 4 chance that they will produce a child with this genotype.

9. The pedigree in **Fig. 7.5c** tracks the presence of dimples through a family's generation. Having dimples is an autosomal dominant trait.

   If individuals II-1 and II-2 have a fourth child, what is the probability that the child will have dimples? **Check your answer in footnote**[9]

   a. 25%
   b. 50%
   c. 75%
   d. 100%

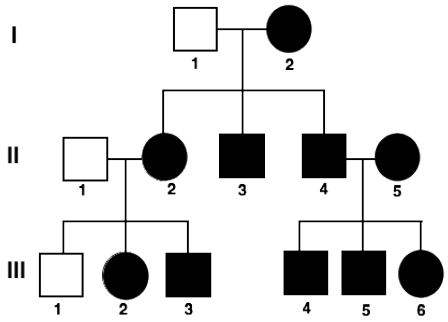

Fig. 7.5c Presence of dimples.

10. The pedigree in **Fig. 7.5c** tracks the presence of dimples through a family's generation. Having dimples is an autosomal dominant trait.What is the phenotype of individual III-4? **Check your answer in footnote**[10]

    a. Dimples
    b. No dimples
    c. dd
    d. DD

11. The pedigree in **Fig. 7.5c** tracks the presence of dimples through a family's generation. Having dimples is an autosomal dominant trait.Which of the following individuals is correctly matched with its genotype? **Check your answer in footnote**[11]

    a. I-1 → **Dd**
    b. II-3 → **dd**
    c. II-2 → **DD**
    d. III-2 → **Dd**

12. The pedigree in **Fig. 7.5c** tracks the presence of dimples through a family's generation. Having dimples is an autosomal dominant trait.If individual III-3 married a woman who was heterozygous for dimples, what is the percent chance their children will have dimples? **Check your answer in footnote**[12]

    1. 0%

---

9. b. A cross between II-1 and II-2 would produce two boxes with dimpled offspring (**Dd**) and two boxes with non-dimpled offspring (**dd**).

10. a. Because we are tracking dimples, shaded individuals represent those who have dimples.

11. d. Individual III-2 has dimples, meaning she must have 1 **D** allele. Her father does not have dimples, so he donates a **d** allele, giving her a genotype of **Dd**.

12. c. This cross has a 3/4 chance of producing individuals that have at least one **D** allele. Because dimples **D** is dominant, these individuals will have dimples.

2. 25%
3. 75%
4. 100%

Step by step solutions

Click to expand the step by step solutions for the above problems

1. If individual III-6 married a man who was homozygous for unattached earlobes, what is most likely to be true regarding their children?
    1. Because the trait we are tracking (attached earlobes) is autosomal recessive, shaded individuals, like III-6, will have a homozygous recessive genotype (**ee**).
    2. If III-6 (**ee**) were to have a child with a man who was homozygous for unattached earlobes (**EE**), then all of the children would be heterozygous – getting one *E* from their father and one *e* from their mother.
       Attached earlobes is a recessive trait and will only occur in **ee** genotypes. Heterozygotes (**Ee**) will have unattached earlobes, as that is the dominant condition.
    3. The correct answer is
       All of their children would have unattached earlobes.
2. If individuals I-1 and I-2 had a fourth child, what is the chance that the child would have attached earlobes?
    1. Because the trait we are tracking (attached earlobes) is autosomal recessive, shaded individuals, like I-2, will have a homozygous recessive genotype (**ee**).
       I-1 must have a heterozygous genotype because he is able to pass on a recessive allele to some of his offspring (II-2 and II-4).
    2. If I-1 and I-2 had another child, the cross would be:

–	**E**	**e**
e	Ee	ee
e	Ee	ee

       Only offspring with **ee** genotypes will have attached earlobes (2/4 boxes).
       $2 \div 4 = 0.5 = 50\%$
    3. The correct answer is 50%
3. What is the genotype of individual I-1?
    1. Individual I-1 is represented by a non-shaded square, indicating that it is a male with unattached

earlobes.

2. Because the trait we are tracking, attached earlobes, is autosomal recessive, shaded individuals will have a homozygous recessive genotype (**ee**).
   Individuals that are non-shaded will have at least one **E** allele.
3. I-1 has children with attached earlobes (II-2 and II-4 are **ee**), meaning he must be able to pass on at least **e** allele. However, he shows the dominant condition, so he must also have one **E** allele.
   Therefore, his genotype is **Ee**.
4. The correct answer is **Ee**

4. What is the genotype of individual II-3?
   1. Individual II-3 is represented by a non-shaded square, indicating that it is a male with unattached earlobes.
   2. Because the trait we are tracking, attached earlobes, is autosomal recessive, shaded individuals will have a homozygous recessive genotype (**ee**).
      Individuals that are non-shaded will have at least one **E** allele.
   3. II-3 has a mother with attached earlobes (**ee**), meaning he must get one **e** allele from her. However, he shows the dominant condition, so he must also have one **E** allele.
      Therefore, his genotype is **Ee**.
   4. The correct answer is **Ee**
5. If individuals I-1 and I-2 had another son, what is the chance that he would have DMD?
   1. Individual I-2 is represented by a shaded circle, indicating that it is an affected female.
      Therefore, she must have a homozygous recessive genotype of X^dX^d
   2. Because males always get their X chromosome from their mother, all of the sons that individual 2 has will receive a recessive X^d allele.
   3. Males will also receive their Y chromosome from their father, giving any son of individuals I-1 and I-2 a genotype of X^dY
   4. The correct answer is 100%.
6. Based on the pedigree, which of the following is true?
   1. Unaffected males, such as individual II-1 have a genotype of X^DY.
      On the other hand, affected males, such as individual II-3, have a genotype of X^dY.
      Since males only have one X chromosome, they cannot be carriers.
   2. Individuals II-4 and II-5 are both shaded in, indicating that they are affected.
      In order to be affected, they must have the recessive genotypes X^dY and X^dX^d. This means that any child they have will have DMD because each parent can only pass on a recessive DMD allele.
   3. Individual III-1 is an unaffected male, meaning that he has a genotype of X^DY.
      If he mates with an unaffected, non-carrier female (X^DX^D), there is no chance that the children will inherit the DMD allele.
   4. The correct answer is

If individual III-1 marries an unaffected, non-carrier female, none of their offspring will have DMD.

7. What is the genotype of individual II-2?
    1. Individual II-2 is represented by a non-shaded circle, indicating that it is an unaffected female.
    2. In order for individual II-2 to have a normal phenotype, but also produce an affected son, she must be a carrier for DMD. This means that she has one of each allele, X^DX^d.
    3. The correct answer is X^DX^d
8. If individual II-3 has a child with a carrier woman, what is the percent chance that the child will be a daughter with DMD?
    1. Individual I-3 is represented by a shaded square, indicating that it is an affected male. Therefore, he must have a genotype of X^dY.
       If he has a child with a DMD carrier (X^DX^d), the cross would be:

–	**X^D**	**X^d**
X^d	X^DX^d	X^dX^d
Y	X^DY	X^dY

    2. In order for a daughter to be affected, her genotype must be X^dX^d.
       Only one box has this genotype, so the chances of having an affected daughter is: ¼ =25%
    3. The correct answer is 25%
9. If individuals II-1 and II-2 have a fourth child, what is the probability that the child will have dimples?
    1. Because the trait we are tracking, dimples, is autosomal dominant, any *shaded* individuals will have at least one dominant allele (**D**).
       Any *unshaded* individuals will have the recessive genotype (**dd**).
    2. II-2 has dimples, meaning she must have at least one **D** allele. In addition, she has a recessive parent, and one of her children has no dimples (**dd**), so she must also have at least one **d** allele. This makes her genotype **Dd**.
       Individual II-1 has no dimples, meaning that he must have a homozygous recessive genotype (**dd**).
    3. Now that we know their genotypes, if we perform a cross between individuals II-1 and II-2 we find:

–	**D**	**d**
d	Dd	dd
d	Dd	dd

2÷4=50%

4. The correct answer is 50%.

10. What is the phenotype of individual III-4?
    1. Phenotype is the physical characteristic that we see (ex: dimples).
       A genotype is the allele combination (ex: DD)
    2. Because the trait we are tracking is having dimples, shaded individuals, like III-4, have dimples.
       Unshaded individuals, like III-1, do not have dimples.
    3. The correct answer is Dimples
11. Which of the following individuals is correctly matched with its genotype?
    1. The trait that we are tracking, dimples, appears to be dominant, as all offspring who have the trait have an affected parent.
       Having dimples also does not skip a generation, which suggests that it is likely dominant.
    2. Shaded individuals have dimples, meaning that they must have at least one **D** allele.
       Unshaded individuals, like I-1, do not have dimples, meaning that they must have the homozygous recessive genotype **dd**.
    3. An individual with dimples can be either **DD** or **Dd**.
       Individuals like II-2, II-3, and III-2 all have at least one recessive parent. Since the recessive parent can only donate a **d**, each of them must have a **d** in their genotype.
       Because they all have dimples, we know they must have one **D** allele as well, giving them all the genotype of **Dd**.
    4. The correct answer is III-2 → **Dd**
12. If individual III-3 married a woman who was heterozygous for dimples, what is the percent chance their children will have dimples?
    1. Because the trait we are tracking (dimples) is autosomal dominant, any *shaded* individuals have at least one dominant allele (**D**).
       Any *unshaded* individuals have the recessive genotype (**dd**).
    2. Individual III-3 must be heterozygous (**Dd**) because he has an unshaded father (**dd**).
       If he was to have a child with a woman who was heterozygous for dimples (**Dd**), then the cross would be:

–	**D**	**d**
D	DD	Dd
d	Dd	dd

    3. Dimples is a dominant trait and will occur whenever a dominant allele is present in the genotype.
       Homozygous recessive individuals (**dd**) will have no dimples, as that is the recessive condition.
       Looking at the Punnett square, we find that ¾ =75% offspring will have at least one **D** allele.
    4. The correct answer is 75%

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7.5 GROUP DISCUSSION

Assignment – Group Discussion

This week students will engage in group discussions on Blackboard. Students will be randomly assigned to groups. See the Blackboard course shell for assignment directions and rubric. Students may also want to use this unit and unit 11 to work on their case study assignment.

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